

MEDIZINISCHE HOCHSCHULE HANNOVER

Institut für Experimentelle Pathologie

Prof. Dr. med. Dr.h.c. U. Mohr

Zentrum Pathologie und Rechtsmedizin

MHH - Exp. Pathologie - D-30623 Hannover

Dr. C.W. Jameson

National Toxicology Program

Report on Carcinogens

MD EC-14

P.O. Box 12233

Research Triangle Park, NC 27709

USA

BY REGISTERED MAIL

Tel:
(+49) 511-532 4523

Fax:
(+49) 511-532 4521

Hannover
2 April 1998

Dear Dr. Jameson,

I have just seen the announcement in the Federal Register dated 19 March, 1998, requesting comments regarding the petition to delist saccharin from the Report on Carcinogens. I was astonished to see that the NTP Board Subcommittee voted 4:3 not to delist saccharin from the Report.

As a long-time cancer researcher and one who has worked with artificial sweeteners, including saccharin, I was very surprised at the decision. I was on the review panel for the original Canadian study on 7 March, 1977, in Ottawa, and for the 1983 review published in Food Chemical Toxicology in 1985. It is my understanding from reading the transcript that two major issues were discussed: one pertaining to the human epidemiology and the other bladder implantation.

It is stated in "Food, Nutrition and the Prevention of Cancer: a Global Perspective" published by the World Cancer Research Fund in association with the American Institute for Cancer Research, July 1997, that:

"Based on the large amount of epidemiological data, the evidence shows that saccharin probably has no relationship with the risk of bladder cancer in the amounts obtainable from normal diets"

which is in agreement with most epidemiologists throughout the world.

In a letter to Dr. Gary Flamm, Center for Food Safety and Applied Nutrition, U.S.F.D.A., Washington, dated 17 April, 1978, I said that:

"In summary, it is my opinion that the treatment with saccharin or cyclamate did not enhance nor depress the carcinogenicity of MNU under these experimental conditions."

Due to our findings over the years, we stopped further research on sweeteners and I brought all the slides to the U.S.A., as requested by the F.D.A., leaving them with Dr. Flamm. They were never returned to me and I was not told the purpose for which they were used. I wonder whether this procedure was correct and according to GLP requirements. Should you not be able to locate this letter, we would be pleased to send you a copy.

A statement from the F.D.A.-funded Mitre Report MTR-87W218, May 1987, on "Relevance of Direct Bladder Exposure Studies to Human Health Concerns":

"Both types of direct bladder exposure studies, pellet implantation and intravesicular catheterization, are considered unsuitable for predicting human carcinogenic risk. These studies should not be applied to the human situation because (1) the study protocols are not validated within experimental species, and (2) the results of these studies cannot be meaningfully extrapolated to humans due to (a) species differences in responses to carcinogens, types of lesions, and physiology, and (b) inappropriate route of exposure."

should also be taken into account.

Collectively, mechanistic research on rodent bladder cancer over the last 20 years has clearly shown that the mechanism related to saccharin is not relevant for humans. The mechanism is associated with a number of chemical substances and is recognized by the scientific community at large, which is consistent with the vote by RG1 and RG2.

It is important that sound science is used to determine which chemicals are listed in the Report on Carcinogens in order to be credible within the global scientific community.

Hopefully, this aberrant decision can be rectified with further evaluation.

Yours sincerely,

A handwritten signature in black ink, appearing to read 'Ulrich Mohr', with a stylized, cursive script.

Prof. Dr. Ulrich Mohr

cc: Dr. Ken Olden, Director, NTP